

**What is claimed is:**

1. A prototype hepatitis B virus vector comprising two novel *cis*-acting elements  
5 essential for hepatitis B virus genome replication, consisting of an  $\alpha$  element and a  $\beta$   
element, whose nucleotide sequences are described in SEQ ID 1 and 2, respectively.
- 10 2. The prototype hepatitis B virus vector of claim 1, wherein said the nucleotide  
sequence is described in SEQ ID 3, comprising, in the 5' to 3' direction, the  
cytomegalovirus immediate early promoter, the DR1, the epsilon, the  $\alpha$  element, the  
DR2 , the  $\beta$  element, and the DR1 element.
- 15 3. The prototype hepatitis B virus vector of claim 2, wherein said the insertion site  
is selected between the 5' epsilon and the  $\alpha$  element.
- 20 4. The prototype hepatitis B virus vector of claim 2, wherein said the insertion site  
is selected between the  $\alpha$  element and the DR2
- 25 5. The prototype hepatitis B virus vector of claim 2, wherein said the vector further  
comprises an endogenous viral promoter.
- 30 6. The prototype hepatitis B virus vector of claim 2, wherein said the viral  
promoter is selected from the group consisting of the core promoter and the pre-S2/S  
promoter, respectively.
7. The prototype hepatitis B virus vector of claim 2, wherein said nucleotide  
sequences up to 0.90 K bp can be inserted between the 5' epsilon and the  $\alpha$  element  
without exceeding the wild-type genome size of the 3.2 K bp.
- 35 8. The prototype hepatitis B virus vector of claim 2, wherein said nucleotide  
sequences up to 1.7 K bp can be inserted between the  $\alpha$  element and DR2 element  
without exceeding the wild-type genome size of the 3.2 K bp.
- 40 9. The prototype hepatitis B virus vector of claim 2, wherein said the vector is  
replication defective.

10. The recombinant hepatitis B virus vector comprising heterologous sequences which express at least one functional heterologous gene product.

5        11. A helper plasmid that expresses the viral proteins essential for the viral genome replication, but lacks encapsidation signal, epsilon element.

12. A method for making a recombinant hepatitis B virus particles, said method comprising:

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a) providing:

15        i) a recombinant hepatitis B virus vector comprising all *cis*-acting elements and heterologous sequences wherein said recombinant genome is capable of expressing at least one functional heterologous gene product and wherein said recombinant genome lacks the ability to produce at least one viral product required for packaging and producing said recombinant vector;

20        ii) a HBV packaging plasmid capable of providing *in trans* hepatitis B virus gene products sufficient to complement said recombinant viral genome lacking the ability to produce at least one viral product required for packaging and producing;

iii) a liver cell in vitro; and

25        b) introducing said recombinant hepatitis B vector and said packaging plasmid into said liver cell under conditions such that said recombinant hepatitis vector is encapsidated into viral particles.

13. The methods of claim 12, wherein said liver cell is selected from the group consisting of human liver cells, mammalian liver cells, avian liver cells, and rodent liver cells.

30        14. A method for transducing target cells with said recombinant hepatitis B virus particles, said method comprising:

the step of introducing said recombinant hepatitis B virus particles into liver tissue of individuals via intravenous or intrahepatic administration.

15. The method of claim 14, wherein said population of target cells are human  
5 hepatocytes.

16. The method of claim 14, wherein said foreign gene is selected from the group consisting of genes encoding anti-sense strand of host genes as well as viral genes including hepatitis B virus and hepatitis C virus. Also included are foreign genes  
10 encoding tumor suppressors, growth factors, hormones, cytokines, coagulation factors, and cellular receptors for various ligands.

17. A method for transducing target cells with said recombinant hepatitis B vector DNA, said method comprising:

15 the step of administrating said recombinant hepatitis B vector DNA into liver tissue of individuals who are chronically infected with hepatitis B virus,

18. The method of claim 17, wherein said population of target cells are human  
hepatocytes.

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19. The method of claim 17, wherein said foreign gene is selected from the group consisting of genes encoding anti-sense strand of host genes as well as viral genes including hepatitis B virus and hepatitis C virus. Also included are foreign genes  
25 encoding tumor suppressors, growth factors, hormones, cytokines, coagulation factors, and cellular receptors for various ligands.